Original Articles

Relationships between JAK2 mutation and clinical characteristics of patients with Philadelphia–negative myeloproliferative neoplasm

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Abstract

Introduction: Philadelphia-negative chronic myeloproliferative neoplasms (Ph-negative MPN) which include polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF) are known to have a propensity to develop thrombosis, bleeding, myelofibrosis and acute leukemia. Objective of this study was to evaluate the prevalence and significance of JAK2 mutation in Ph-negative MPN patients and evaluate the prognostic factors leading to morbidity and mortality.

Method: This study included retrospective reviews of Ph-negative patients diagnosed and treated in the Hematology Divisions of Rajvithee and Thammasat Hospitals, Thailand from 1 January 2002 to 31 December 2011. JAK2 mutation was established by allele-specific polymerase chain reaction (PCR).

Result: There were 73 Ph-negative MPN patients including 28 with ET, 44 with PV, and 1 with PMF. The incidence of JAK2 mutation was 54.8% (40/73 cases), 61% in PV patients (27/44 cases) and 46.4% in ET patients (13/28 cases). The significant factor associated with positive JAK2 mutation was age over 59 years (OR 2.06, 95%CI=1.59 - 11.45, p = 0.003). Other factors had no statistical significance. A white blood cell count (WBC) of over 12,000/mm^3 and a platelet count of over 400,000/mm^3 presented as major risks for bleeding complications in PV patients. (OR 1.36, 95%CI=1.09 - 1.69, p = 0.008 and OR 1.38, 95%CI=1.10 - 1.73, p = 0.006, respectively).

Discussion and Conclusion: This study showed having an age of atleast 59 years was associated with a high rate of JAK2 mutation. Elevated WBC counts and platelet counts correlated well with increased bleeding in PV patients.

Key words: Myeloproliferative neoplasm, Polycythemia vera, Essential thrombocythemia, JAK2 mutation, JAK2V617F mutation

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Introduction

Polycythemia vera (PV), essential thrombocythemia (ET) and primary myelofibrosis (PMF) are Philadelphia (Ph) chromosome-negative chronic myeloproliferative neoplasms (MPNs) by the definition of World Health Organization (WHO) Classification of Tumors of Hematopoietic and Lymphoid Tissues 2008 revision.[1] Patients usually present with high cellular levels leading to bleeding, thrombosis, and may turn into acute leukemia or primary myelofibrosis (PMF). PMF is a rare condition presented commonly with splenomegaly. The identification of the JAK2 mutation has been an exciting new discovery in Ph-negative MPNs since 2005.[2 - 3] The most common mutation was JAK2V617F mutation which can be detected at rates of about 23 - 95%,[2 – 4] and higher in patients with PV (65 - 97%) than ET and PMF (20 - 65%).[5 - 6] However, JAK2V617F mutation was also reported in lower frequencies in other hematologic malignancies[7] and possible consequences of the JAK2V617F and the development of JAK2 in MPN are still under active investigation.[8 - 10] There are few studies about JAK2 mutation and clinical symptoms of Ph negative MPNs in Thailand.[11]

The primary objective of this study was to determine the incidence of JAK2 mutation in Ph-negative MPN patients. The secondary objective was to find possible correlations between clinical and laboratory parameters with JAK2 mutation in those patients and any other potential significance.

Methods

This study included retrospective reviews of Ph-negative MPN patients who were diagnosed by WHO 2008 criteria[12] and treated at the Hematology Divisions of Rajvithee and Thammasat Hospitals from 1 January 2002 to 31 December 2011. JAK2 mutation was detected by allele specific polymerase chain reaction (PCR). Odds ratio (OR) and Fisher's Exact Test were used for statistical analysis. The freqeuncy of JAK2 mutation and its correlation with patients' clinical and laboratory parameters were then analyzed.

The patients who were not Ph-negative MPN or who did not sign a consent for JAK2 mutation analysis were excluded from the study.

Results

From 1 January 2002 to 31 December 2011, there were 73 Ph-negative MPN patients: 28 with ET, 44 with PV and 1 with PMF as shown in Table 1. From all 73 Ph-negative MP N patients, there were 44 males (60.3%), with the mean aged of 58.4 years (20 - 94 years). From the forty-four patients with PV, there were 27 males (61.4%), aged 22 - 87 years (mean 57.7 years), and 17 males from 28 ET patients (61.4%), aged 22 - 87 years (mean 57.7 years). There was one PMF female patient, 70 years old.

Table 1 Characteristics and treatment of Ph negative MPN patients

Parameter	PV N = 44	ET N = 28	PMF N = 1	All N = 73
Age: average (years) (range)	57.7 (22 - 87)	59.56 (20 - 94)	70	58.44 (20 - 94)
Male/ total case	27/44	17/27	0	44/73
Hb (g/dL)	16.34 (5.9 - 23.9)	12.69 (7.8 - 16.6)	7.8	14.89 (5.9 - 23.9)
Hct (%)	50.2 (21.2 - 73.7)	38.37 (27.7 - 50)	23.6	45.5 (21.2 - 73.7)
WBC (/mm^3)	17,819	13,721	35,200	16,141
	(6,400 - 51,500)	(3,700 - 35,200)		(3,700 - 51,500)
Platelet (/mm^3)	639,409	1,151,786	160,000	829,370
	(175,000 - 1,765,000)	(485,000 -1 ,123,000)		(160,000 - 2,123,000)
Splenomegaly (cm)	8	1	1	10
Treatment	cases	cases	cases	cases
Hydroxyurea	42	26	0	68
Anagrelide	7	2	0	9
Aspirin	36	22	0	58
Complications				
Thrombosis	20	8	0	28
Bleeding	8	2	0	10
Leukemia	2	0	0	2
Myelofibrosis	1	1	1	2

Laboratory findings in the 44 PV patients showed a mean hemoglobin (Hb) level of 16.34 g/dL (range, 5.9 - 23.9 g/dL) with a mean hematocrit (Hct) of 50.2% (range, 21.2 - 73.7%). There were 2 patients with anemia (4.5%) and the level of HB/Hct increased after iron supplementation. For the 28 ET patients, mean Hb level was 12.69 g/dL (range, 7.8 - 16.6 g/dL). There were 8 patients with anemia (28.5%) and the level of Hb increased after iron supplementation.

The mean level of WBC was 17,819/mm^3 (range, 6,400 - 51,500 mm^3) in PV patients and 13,721/mm^3 (range, 3,700 - 35,200/mm^3) in ET patients. PV patients had a mean platelet count at 639,409/mm^3 (range, 175,000 - 1,765,000/mm^3), and the mean platelet count was 1,151,786/mm^3 (range, 485,000 - 1,123,000/mm^3) in ET patients. One patient with PMF had a Hb level of 7.8 g/dL, a Hct level of 23.6%, a WBC count of 35,200/mm^3, and a platelet count of 160,000/mm^3.

There was an 18% (8 in 44 cases) splenomegaly in PV patients and 4% (1 in 28 cases) in ET patients. One patient with PMF presented with an enlarged spleen. The most common complication found was thrombosis. There were 20 cases in the 44 cases (45%) in the PV group and 8 cases in the 28 cases (7%) in the ET group with thrombosis. Bleeding problems were found in 8 cases out of 44 cases (18%) in the PV group and 2 cases out of 28 cases (7%) in the ET group.

Almost all patients (68 out of 73; 93%) received hydroxyurea for general cytoreduction treatment. A few cases received anagrelide (9 out of 73; 12%), and 80% received aspirin (58 out of 73 cases).

Table 2 Patient factors and correlation with JAK2 mutation in Ph-negative MPN patients

	All cases (n = 73)		OR	p-value
	JAK-	JAK+	(95%CI)	
Age				
≥ 60 yr	10 (30.3%)	26 (65.0%)	4.27	0.003
< 60 yr	23 (69.7%)	14 (35.0%)	(1.59 - 11.45)	
Female	15 (45.5%)	14 (35.0%)	1.55	0.36
Male	18 (54.5%)	26 (65.0%)	(0.60 - 3.98)	
Duration from diagnosis				
≥ 5 yr	14 (42.4%)	23 (57.5%)	1.83	0.20
< 5 yr	19 (57.6%)	17 (42.5%)	(0.72 - 4.66)	
WBC				
≥ 12,000/mm^3	18 (54.5%)	28 (70.0%)	1.94	0.17
< 12,000/mm^3	15 (45.5%)	12 (30.0%)	(0.74 - 5.09)	
Platelet ≥ 400,000/mm^3	25 (75.8%)	32 (80.0%)	1.28	0.66
	8 (24.2%)	8 (20.0%)	(0.42 - 3.89)	
Platelet ≥ 800,000/mm^3	13 (39.4%)	19 (47.5%)	1.39	0.48
	20 (60.6%)	21 (52.5%)	(0.54 - 3.54)	
Thrombosis	9 (27.3%)	19 (47.5%)	2.4	0.07
	24 (72.7%)	21 (52.5%)	(0.90 - 6.47)	
Bleeding	2 (6.1%)	8 (20.0%)	3.87	0.07
	31 (93.9%)	32 (80.0%)	(0.76 - 19.70)	
Splenomegaly:				
yes	3 (9.1%)	8 (20.0%)	2.5	0.18
no	30 (90.9%)	32 (80.0%)	(0.60 - 10.32)	
Turn to AL:				
yes	2 (6.1%)	0	NA	0.72
no	31 (93.9%)	40 (100%)		
Turn to MF:				
yes	1 (3.0%)	1 (2.5%)	0.82	0.89
no	32 (97%)	39 (97.5%)	(0.05 - 13.64)	

Abbrevations: AL, acute leukemia; MF, myelofibrosis

Table 3 Patient factors and correlation with JAK2 mutation in PV patients

	PV (44 cases)		OR	p-value
	JAK- (17)	JAK+(27)	(95%CI)	
Age				
≥ 60 yr	3 (17.6%)	18 (66.7%)	9.33	0.001
< 60 yr	14 (82.4%)	9 (33.3%)	(2.12 - 41.06)	
Female	9 (52.9%)	8 (29.6%)	2.67	0.12
Male	8 (47.1%)	19 (70.4%)	(0.76 - 9.43)	
Duration from diagnosis				
≥ 5 yr	10 (58.8%)	9 (33.3%)	1.40	0.60
< 5 yr	7 (41.2%)	18 (66.7%)	(0.40 - 4.9)	
WBC				
≥ 12,000 /mm^3	11 (64.7%)	19 (70.4%)	1.29	0.70
< 12,000 /mm^3	6 (35.3%)	8 (29.6%)	(0.36 - 4.7)	
Platelet ≥ 400,000/mm^3	10 (58.8%)	19 (70.4%)	1.63	0.43
	7 (41.2%)	8 (29.6%)	(0.47 - 5.9)	
Platelet ≥ 800,000/mm^3	4 (23.5%)	10 (37.0%)	1.9	0.34
	13 (76.5%)	17 (63.0%)	(0.48 - 7.4)	
Thrombosis	5 (29.4%)	15 (55.6%)	3	0.86
	12 (70.6%)	12 (44.4%)	(0.83 - 10.9)	
Bleeding	1 (5.9%)	7 (25.9%)	5.6 (0.62 - 50.34)	0.07
	16 (94.1%)	20 (74.1%)		
Splenomegaly:				
yes	1 (5.9%)	7 (25.9%)	5.6 (0.63 - 50.3)	0.73
no	16 (94.1%)	20 (74.1%)		
Turn to AL:				
yes	2 (11.8%)	0	NA	0.47
no	15 (88.2%)	27 (100%)		
Turn to MF:				
yes	1 (5.9%)	0	NA	0.16
no	16 (94.1%)	27 (100%)		

Abbrevations: AL, acute leukemia; MF, myelofibrosis

Table 4 Patient factors and correlation with JAK2 mutation in ET patients

	ET (29 cases)		OR	p-value
	JAK-	JAK+	(95%CI)	
Age				
≥ 60 yr	7 (43.8%)	8 (61.5%)	2.06	0.33
< 60 yr	9 (56.3%)	5 (38.5%)	(0.46 - 9.14)	
Female	6 (37.5%)	6 (46.2%)	0.7	0.63
Male	10 (62.5%)	7 (53.8%)	(0.16 - 3.10)	
Duration from diagnosis				
≥ 5 yr	4 (25.0%)	5 (38.5%)	1.87	0.44
< 5 yr	12 (75.0%)	8 (61.5%)	(0.38 - 9.19)	
WBC				
≥ 12,000/mm^3	7 (43.8%)	4 (30.8%)	2.89	0.16
< 12,000/mm^3	9 (56.3%)	4 (30.8%)	(0.62 - 13.45)	
Platelet ≥ 400,000/mm^3	15 (93.8%)	13 (100%)	1.87	0.27
	1 (6.3%)	0	(01.36 - 2.63)	
Platelet ≥ 800,000/mm^3	9 (56.3%)	9 (69.2%)	1.7	0.47
	7 (43.8%)	4 (30.8%)	(0.38 - 8.14)	
Thrombosis	12 (75%)	9 (69.2%)	1.3	0.73
	4 (25%)	4 (30.8%)	(0.26 - 6.82)	
Bleeding	1 (6.3%)	1 (7.7%)	1.25	0.88
	15 (93.8%)	12 (92.3%)	(0.07 - 22.13)	
Splenomegaly:				
yes	2 (12.5%)	1 (7.7%)	0.58	0.67
no	14 (87.5%)	12 (92.3%)	(0.47-7.26)	
Turn to AL:				
yes	0	0	NA	NA
no	16 (100%)	13 (100%)		
Turn to MF:				
yes	0	12 (92.3%)	NA	0.19
no	16 (100%)	1 (7.7%)		

Abbrevations: AL, acute leukemia; MF, myelofibrosis

The incidence of JAK2 mutation was 54.8% (40/73 cases), 61% in PV patients (27/44 cases) and 46.4% in ET patients (13/28 cases). One factor associated with positive JAK2 mutation was an age at least 60 years (OR 2.06, 95%CI=1.59 - 11.45, p = 0.003) as illustrated in Table 2, 3 and 4. Other factors were not statistically significant. A WBC count of over 11,999/mm^3 and platelet count of over 399,999/mm^3 were shown as major risk factors for bleeding complications (OR 1.36, 95%CI = 1.09 - 1.69 p = 0.008 and OR 1.38, 95%CI = 1.10 - 1.73, p = 0.006, respectively).

This study of the correlation of clinical factors including JAK2 mutation together with thrombosis, bleeding, incidence of acute leukemia and myelofibrosis transformations found that a WBC count of at least 12,000/mm^3 and a platelet count of at least 400,000/mm^3 in PV patients suggested an increased risk of bleeding problems (OR 1.32, 95%CI=1.09 - 1.69, p = 0.008 and OR 1.38, 95% CI =1.10 - 1.73, p = 0.006, respectively). Although other factors detailed in Table 5.1 and 5.2 also had high OR; they were not statistically significant (p > 0.05).

Discussion and Conclusion

Since William Dameshek introduced the spectrum of myeloproliferative disorder in 1951[13], the discovery of the JAK2 mutation in 2005[8] led to an increase of knowledge in pathophysiology, a new guideline for diagnosis, and more hope in the treatment of MPN.[14 - 15] There were many studies reporting the incidence of JAK2 mutation ranging from 65 - 97% in PV [6, 7 - 16] and from 23 - 57% in ET and PMF patients.[8, 17 - 18] In this study, we found that the incidence of JAK2 mutation was 61% in PV patients and 46% in ET patients. One patient with PMF had a positive JAK2 mutation. However, the effects of the JAK2 mutation to clinical presentation cannot be determined in this case. The risk of bleeding, thrombosis or other cardiovascular disease must be evaluated by using an age and a history of thrombosis event.

Dahabresh et al.[19] showed the results of meta-analysis from 17 studies about Ph-negative MPN patients that patients with JAK2 mutation had a correlation with a higher incidence of thrombosis (~ 90%) which are both thrombosis leading to diagnosis and during treatment (OR = 1.68, 95%CI=1.30 - 2.15, p < 0.0001 and OR 2.5, 95%CI=1.71 - 3.66, p < 0.0001, respectively). The risk of thrombosis was found in arterial and venous sites. No clinical correlation was found between the JAK2 mutation and bleeding incidence or incidence of transformation to acute leukemia and myelofibrosis. In addition, they found that splenomegaly may be associated with the JAK2 mutation (OR 1.32, 95%CI = 1 - 1.75, p = 0.06). ET patients with JAK2 mutation were presented in a high proportion of cases turning into PV (OR = 7.67 (95%CI=2.04 - 28.87), p = 0.0009).[17] The presence of JAK2 mutation did not necessarily affect the incidence of transformation to acute leukemia (OR = 1.44 (95%CI=0.54 - 3.82), p = 0.62) or myelofibrosis (OR = 0.64 (95%CI=0.33 - 1.23), p = 0.24) in this study.

Kittlur et al.[18], Cheung et al[20], Zhang et al[21] and James et al.[22] reported that ET patients with JAK2 mutation had a higher Hb or Hct levels like PV, or had a chance of polycythemic laboratory profile such as high Hb, leukocytosis, and low erythropoietin level. Many studies reported that the incidence of thrombosis was as high as 90% in ET patients who had JAK2 mutation.[9, 23 - 30]

Passamonti et al.[31] reported life expectancy and prognostic factors for survival in patients with PV and ET. PV patients had an overall survival rate of 73% at 15 years post diagnosis. High-risk patients were defined by a history of thrombosis (HR = 2.2, p = 0.002 for PV) and thrombocytosis (HR = 2, p = 0.01 for PV) and male gender (HR 1.8, p = 0.03 for ET). Najean et al.[32] reported that the incidence of acute leukemia and myelofibrosis transformation in PV and ET patients was quite low at 7% in PV and 2% in ET patients at 15 years, but it was difficult to differentiate from the effects of immunosuppressive drug such as pipobroman or hydroxyurea.

Table 5.1 Correlation of clinical factors and complication

	ODDs ratio (95% CI)					
	Thrombosis	p	Bleeding	p	Splenomegaly	p
Age ≥ 60 year						
All	1.67 (0.64 - 4.3)	0.29	1.03 (0.27 - 3.9)	0.96	1.9 (0.53 - 7.5)	0.35
PV	1.7 (0.52 - 5.67)	0.37	2.08 (0.43 - 10.06)	0.59	2.08 (0.85 - 1.5)	0.35
ET	1.83 (0.35 - 9.71)	0.47	0.86 (0.69 - 1.06)	0.80	2.0 (0.16 - 24.87)	0.58
WBC ≥ 12,000/mm^3						
All	1.83 (0.66 - 5.02)	0.23	6.3 (0.75 - 53)	0.38	3.04 (0.60 - 15.27)	0.14
PV	1.16 (0.33 - 4.2)	0.81	1.36 (1.09 - 1.69)	0.008	3.9 (0.44 - 35.81)	0.17
ET	3.3 (0.54 - 20.27)	0.18	0.8 (0.45 - 14.16)	0.88	1.7 (0.14 - 21.33)	0.67
PLT ≥ 400,000/mm^3						
All	0.75 (0.24 - 2.3)	0.61	1.2 (0.24 - 2.3)	0.02	1.31 (0.25 - 6.8)	0.74
PV	0.93 (0.27 - 3.24)	0.91	1.38 (1.10 - 1.73)	0.006	4.45 (0.49 - 40.19)	0.13
ET	1.4 (1.11 - 1.77)	0.42	1.08 (0.97 - 1.19)	0.70	14 (3.68 - 53.23)	0.03
PLT ≥ 800,000/mm^3						
All	1.19 (0.46 - 3.07)	0.73	1.33 (0.35 - 5)	0.67	1.08 (0.29 - 3.92)	0.91
PV	2.0 (0.55 - 7.24)	0.29	5.0 (0.99 - 25.21)	0.046	2.60 (0.54 - 12.45)	0.24
ET	1.03 (0.19 - 5.51)	0.98	0.82 (0.62 - 1.08)	0.042	0.27 (0.02 - 3.33)	0.29
JAK2, All	2.4 (0.90 - 6.47)	0.07	3.87 (0.76 - 19.70)	0.07	2.5 (0.60 - 10.32)	0.18
JAK2, PV	3 (0.83 - 10.9)	0.86	5.6 (0.62 - 50.34)	0.07	5.6 (0.63 - 50.3)	0.73
JAK2, ET	1.3 (0.26 - 6.82)	0.73	1.25 (0.07 - 22.13)	0.88	0.58 (0.47 - 7.26)	0.67

PV = polycythemia vera

ET = essential thrombocythemia

Table 5.2 Correlation of clinical factors and complication

	ODDs ratio (95% CI)			
	Turn to AL	p	Turn to MF	p
Age ≥ 60 year,				
All	0.94 (0.87 - 1)	0.09	1.03 (0.62 - 17.09)	0.98
PV	0.9 (0.8 - 1.04)	0.10	0.95 (0.87 - 1.04)	0.25
ET	NA	-	0.97 (0.33 - 1.0)	0.25
WBC ≥ 12,000/mm^3,				
All	1.04 (0.98 - 1.11)	0.17	1.04 (0.98 - 1.11)	0.17
PV	1.07 (0.97 - 1.18)	0.21	1.03 (0.97 - 1.11)	0.38
ET	NA	NA	1.07 (0.94 - 1.21)	0.27
PLT ≥ 400,000/mm^3,				
All	1.04 (0.98 - 1.09)	0.32	1.04 (0.98 - 1.09)	0.32
PV	1.07 (0.97 - 1.19)	0.19	1.04 (0.97 - 1.11)	0.36
ET	NA	NA	1.04 (0.97 - 1.11)	0.79
PLT ≥ 800,000/mm^3,				
All	1.2 (0.07 - 21)	0.85	1.06 (0.97 - 1.16)	0.06
PV	2.23 (0.13 - 38.49)	0.59	1.07 (0.93 - 1.25)	0.13
ET	NA	NA	1.06 (0.95 - 1.18)	0.32
JAK2, All	NA	0.72	0.82 (0.05 - 13.64)	0.89
JAK2, PV	NA	0.47	NA	0.16
JAK2, ET	NA	NA	NA	0.19

PV = polycythemia vera

ET = essential thrombocythemia

AL = acute leukemia

MF = myelofibrosis

In this study, we found a higher incidence of complications, such as thrombosis and bleeding, in patients with JAK2 mutation (OR 3 and 5.6 for PV; OR 1.3 and 1.25 for ET, respectively); however, this was no statistically significant, might be due to small sample size. For acute leukemia and myelofibrosis transformation, there were limitations due to the low number of patients, too and the low incidence of transformation of which we could not calculate the correlation, as shown in Table 5.1 and 5.2 We found 5% (2/44) of PV patients had a transformation to acute leukemia, and that 3% (2/72) of all Ph-negative MPN had a transformation to myelofibrosis. Regarding the patients' follow-up, no long term patient follow-ups were presented in all patients, some patients were followed shorter than 1 year, so this study could not determine a true life expectancy. The mean duration of diagnosis and follow-up was 5.6 years in PV patients (1 - 14 years) and 3.8 years in ET patients (1 - 8 years).

In summary, this study is a study of the incidence of JAK2 mutation and the relationship between the mutation and clinical symptoms in Thailand. Our study supports previous studies about the incidence and correlation of the

JAK2V617F mutation. The positive mutation was correlated with age, high Hb and Hct levels, and a tendency to have a leukocytosis, splenomegaly, bleeding and thrombosis events. The detection of this mutation was used for diagnosis and classification, and may be useful in the treatment of MPNs in the near future. The longer follow-up of this study should be done to estimate the life expectancy of Thai patients with PV and ET.

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บทคัดย่อ

ความสัมพันธ์ระหว่างการกลายพันธุ์ของยีน JAK2 และอาการทางคลินิกในผู้ป่วย myeloproliferative neoplasm ซึ่งไม่พบฟิลาเดลเฟียโครโมโซม

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บทนำ: กลุ่มโรค myeloproliferative neoplasm (MPN) ซึ่งไม่พบฟิลาเดลเฟียโครโมโซมประกอบด้วยโรคที่พบบ่อยได้แก่ โรคเลือดข้น (polycythemia vera, PV) โรคเกล็ดเลือดสูง (essential thrombocythemia, ET) และโรคพังผืดในไขกระดูกแบบเกิดเอง (primary myelofibrosis, PMF) ซึ่งเป็นที่ทราบกันว่ามีโอกาสเกิดภาวะลิ่มเลือดอุดตัน เลือดออกผิดปรกติ เกิดพังผืดในไขกระดูก และการเกิดมะเร็งเม็ดเลือดขาวเฉียบพลัน การศึกษานี้มีวัตถุประสงค์เพื่อศึกษาอุบัติการณ์และความสำคัญของการกลายพันธุ์ของยีน JAK2 และอาการทางคลินิกในผู้ป่วย MPN ซึ่งไม่พบฟิลาเดลเฟียโครโมโซม รวมทั้งประเมินปัจจัยที่มีผลต่อการทุพพลภาพหรือการเสียชีวิต

วิธีการศึกษา: การศึกษานี้เป็นการศึกษาย้อนหลังโดยรวบรวมข้อมูลผู้ป่วย MPN ซึ่งไม่พบฟิลาเดลเฟียโครโมโซมที่ได้รับการวินิจฉัยและรักษาในโรงพยาบาลธรรมศาสตร์เฉลิมพระเกียรติ จังหวัดปทุมธานี และโรงพยาบาลราชวิถี กรุงเทพมหานคร ตั้งแต่ ๑ มกราคม พ.ศ. ๒๕๔๕ ถึง ๓๑ ธันวาคม พ.ศ. ๒๕๕๔ การตรวจการกลายพันธุ์ของยีนโดย allele specific PCR

ผลการศึกษา: ตั้งแต่ ๑ มกราคม พ.ศ. ๒๕๔๕ ถึง ๓๑ ธันวาคม พ.ศ. ๒๕๕๔ มีผู้ป่วย MPN ซึ่งไม่พบฟิลาเดลเฟียโครโมโซมจำนวน ๗๓ ราย โดยเป็นผู้ป่วย ET ๒๘ ราย ผู้ป่วย PV ๔๔ ราย และผู้ป่วย PMF ๑ ราย อุบัติการณ์ของการกลายพันธุ์ของยีน JAK2 เท่ากับร้อยละ ๕๔.๘ (๔๐/๗๓ ราย) โดยพบร้อยละ ๖๑ ในผู้ป่วย PV (๒๗/๔๔ ราย) และร้อยละ ๔๖.๔ ในผู้ป่วย ET (๑๓/๒๘ ราย) ปัจจัยที่พบว่าเกี่ยวข้องกับการกลายพันธุ์ของยีน JAK2 ได้แก่ อายุมากกว่า ๕๙ ปี (OR 2.06, 95%CI=1.59 - 11.45, p = 0.003) ปัจจัยอื่นไม่พบว่ามีความสำคัญทางสถิติ นอกจากนั้นพบว่า ปริมาณเม็ดเลือดขาวที่มากกว่า ๑๒,๐๐๐ ลูกบาศก์มิลลิเมตร และเกล็ดเลือดที่มากกว่า ๔๐๐,๐๐๐ ลูกบาศก์มิลลิเมตร เป็นปัจจัยเสี่ยงต่อการเกิดเลือดออกผิดปรกติ (OR 1.36; 95%CI=1.09 - 1.69, p = 0.008 และ OR 1.38; 95%CI=1.10 - 1.73, p = 0.006 ตามลำดับ)

วิจารณ์ และสรุปผลการศึกษา: การศึกษานี้พบว่าผู้ป่วย MPN ที่มีอายุมากกว่าหรือเท่ากับ ๕๙ ปี มีอุบัติการณ์ของการกลายพันธ์ของยีน JAK2 สูงกว่ากลุ่มอายุน้อยกว่า ๖๐ ปี ปริมาณเม็ดเลือดขาวที่มากกว่าหรือเท่ากับ ๑๒,๐๐๐ ลูกบาศก์มิลลิเมตร และเกล็ดเลือดที่มากกว่าหรือเท่ากับ ๔๐๐,๐๐๐ ลูกบาศก์มิลลิเมตร เป็นปัจจัยเสี่ยงต่อการเกิดเลือดออกผิดปรกติ

คำสำคัญ: Myeloproliferative neoplasm, โรคเลือดข้น (polycythemia vera, PV) โรคเกล็ดเลือดสูง (essential thrombocythemia, ET) การกลายพันธุ์ของยีน JAK2, การกลายพันธุ์ของยีน JAK2 ที่ตำแหน่ง V617F